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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/412,297	10/05/1999	KANG TING	3100.006US0	9486

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EXAMINER

FORD, VANESSA L

ART UNIT PAPER NUMBER

1645

DATE MAILED: 03/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

Office Action Summary**Application No.**

09/412,297

Applicant(s)

TING, KANG

Examiner

Vanessa L. Ford

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 November 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-50 is/are pending in the application.
- 4a) Of the above claim(s) 3-7 and 13-49 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,8-12 and 50 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

FINAL ACTION

1. This Office Action is responsive to Applicant's amendment and response filed November 17, 2003. Claim 1 has been amended. Claim 50 has been added.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

Rejection Maintained

3. The rejection of claims 1-2, 8-12 and newly submitted claim 50 under 35 U.S.C. 112, first paragraph is maintained for the reasons set forth on pages 2-8, paragraph 4 of the previous Office Action.

Applicant urges that one embodiment of the specification specifically demonstrates that endogenous Nell expression in osteoprogenitor cells, mesenchymal cells and osteoblastic cell as well as induced expression of Nell-1 in MC3T3 cells and rat fetal calvarial primary cell cultures. Applicant urges that over expression of Nell-1 in the cell cultures lead to enhanced mineralization. Applicant urges that Ting (1999) describes Nell-1 localization primarily in the calvarial osteoprogenitor cells and intramembraneous bone. Applicant urges that Ting discloses *nel* in chick limb development. Applicant urges that Zhang describes Nell-1 expression in bone forming areas of sutures and the calvarium and ossifying membranuous bone in the mandible. Applicant urges that the specification and references cited indicated Nell-1's expression in a variety of osteogenic tissues and correlates to mineralization in

osteogenic cells. Applicant urges that the specification is enabling for the claims presented.

Applicant's arguments filed November 17, 2003 have been fully considered but they are not persuasive. The claims as amended are drawn to a method of screening for an agent that modulates bone mineralization said method comprising contacting an osteogenic cell containing a NELL-1 gene with a test agent; and detecting an expression level of said NELL-1 gene in the contacted cell, where a difference in the expression level of NELL-1 in the contacted cell compared to an expression level of NELL-1 in a cell that has not been contacted indicates that said test agent is an agent that modulates bone mineralization. The specification defines the term "test agent" as an agent that is to be screened in one or more of the assays described herein. The specification teaches that the agent can be virtually a chemical compound that exist as a single isolated compound or can be a member of a chemical library. The specification teaches that the test agent will be a small molecule (pages 8-9). The specification teaches that the test agent is not a nucleic acid or a protein (page 4). The experimental examples of the instant specification merely teaches that the NELL-1 gene is expressed in cranial and intramebraneous bone and neural tissues (page 41). The specification suggests that NELL-1 is closely associated with bone formation (page 42).

The specification fails to enable a method of screening for an agent that modulates bone mineralization. The specification has failed to disclose "test agents" used in the claimed method. The specification merely discloses that the same assays

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that can be used to screen for agents that modulate the expression of NELL-1 can be used to modulate the activity of MT-SP1 serine protease (page 29). Is MT-SP1 serine protease a "test agent" that can be contacted with an osteogenic cell containing a NELL-1 gene that can be used in the claimed method of screening? One of skill in the art could not conclude that the specification is enabled for the claimed method absent the teachings of examples of "test agents" to be used in the claimed method.

In response to Applicant's arguments regarding the prior art references (i.e. Ting et al and Zhang et al), although both references teach that NELL-1 is localized primarily in osteoprogenitor and intramembraneous bone does not establish that NELL-1 is a modulator of bone mineralization since the prior art teaches that the precise function of NELL-1 is unknown. The mere presence of the NELL-1 gene in osteogenic cells does not establish its function. The function of the NELL-1 gene can not be ascertained by the instant disclosure. One of skill in the art could not conclude that the claimed method of screening for an agent that modulates bone mineralization in an osteogenic cell containing a NELL-1 gene can be obtained by the information contained in the instant disclosure.

Factors to be considered in determining whether undue experimentation is required are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

There is lack of enablement for the use of the method for screening an agent that modulates bone mineralization because the specification merely focuses on the enhancement of the NELL-1 gene in fetal calvarial osteoblastic cells. The mere presence of a NELL-1 gene in an osteogenic cell does not establish its function. The state of the art regarding the NELL-1 gene teaches that its function has not been identified. It is determined that there are no working examples commensurate with the claims that demonstrate that a reduction in Nell -1 expression corresponds with decreased bone mineralization and there is limited guidance provided in the specification as to how to use the claimed method. The skilled artisan is forced into undue experimentation to practice (make and use) the invention as claimed.

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

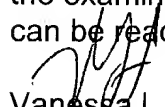
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

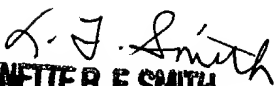
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5. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571)272-0864.


Vanessa L. Ford
Biotechnology Patent Examiner
February 11, 2003


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